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CREUTZFELDT-JAKOB DISEASE IN CANADA

Creutzfeldt-Jakob disease (CJD) is a rare and fatal neurodegenerative disease. The clinical presentation includes dementia, myoclonus and progressive motor dysfunction. Death usually occurs within a year of the onset of symptoms. CJD is transmitted in humans in rare instances, and the disease can be dormant for as long as 30 years. The average age of onset is 60 years, but there are recorded instances of onset as early as 16 years, and as old as 80[1-5]. The causative agent has not been identified, but slow viruses of the central nervous system[5] and infective proteinaceous particles or prions[4] have both been postulated as the agent responsible for the disease. There is no current treatment for CJD. Diagnosis is based on clinical signs, characteristic EEG changes, brain biopsy and postmortem histopathologic findings[1,6]. Genetic predisposition to the disease is associated with mutations in the prion protein gene.

Three distinct types of CJD are recognized. Sporadic-type CJD, which accounts for almost 90% of all cases, may result from spontaneous somatic mutation of a prion protein gene within the host. Familial-type disease results from autosomal dominant inheritance of an affected gene, and constitutes 5% to 10% of all cases. Iatrogenic or acquired CJD is responsible for < 1% of all known cases. In iatrogenic cases, person-to-person transmission has occurred via transfer of tissue from an affected donor (corneal transplant and dura mater grafts), through peripheral injection of pooled cadaveric pituitary gland extract (growth hormone injection and human gonadotropin injection), and by use of contaminated neurosurgical instruments[1-5,7-9].

Concerns have been raised regarding the possible transmissibility of CJD through transfusion of blood or organ transplants. In response to this, the following review of Canadian mortality data has been undertaken to search for clustering of CJD by age, sex or geography.

Incidence of CJD

It is estimated that, worldwide, between 0.5 and 1 case of CJD per million population occurs annually. Increased incidence in some regions of the world has been attributed to familial disease[10]. A recent review of mortality data in the United States has shown that the average annual incidence of CJD in that country is 0.9 deaths per million population[11]. There are no published reports for CJD incidence in Canada.

Transmission of CJD to recipients of blood transfusions or organ transplants would likely result in unusual age, temporal or geographic distributions. The mortality of CJD in Canada was reviewed with this possibility in mind.

The incidence of CJD in Canada cannot be directly measured because the disease is not notifiable. However, because the disease is uniformly fatal and time between onset and death is relatively short, mortality figures can be used to infer population incidence. The Statistics Canada mortality reports for the years 1979 to 1993 were reviewed for CJD deaths by age and sex for each province. Reports before 1979 were not used because CJD (ICD-9 code 46.1) was not listed as a cause of death prior to that year.

Overall, 334 deaths attributed to CJD were recorded in Canada in the 15-year period from 1979 to 1993. The number of deaths ranged from 14 to 34 per year, with a 1.1:1.0 female-to-male ratio (Figure 1).

Cumulative CJD mortality in Canada by province and territory between 1979 and 1993 is shown in Figure 2. Sixty-four percent of deaths occurred in Ontario and Quebec; this is consistent with the population distribution for the country. There is no evidence of clustering of disease by province or territory, but published data are not available by smaller geographic areas. The age distribution for CJD deaths (Figure 3) shows that 50% of the deaths occurred in the sixth decade, corresponding to the peak age of onset for sporadic-type CJD[1-3].

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CJD Transmission in Canada

There is documentation of six cases in Ontario (five deaths and one diagnosed case) recorded between April 1989 and October 1990. Two of these cases had come from areas of Czechoslovakia with a high incidence of familial-type disease, but no other risk factors were associated with these cases[12]. It is likely that most cases of CJD in Canada are of the sporadic type. Familial-type CJD has been documented in several Canadian families of European origin[8]. In the mid-1980s, two cases were reported from one family (mother and son) in British Columbia; this may have been familial-type disease[13]. With reference to iatrogenic disease, although human growth hormone was used in this country from 1965 until April 1985[14], there are no reports of iatrogenic CJD occurring in Canada (Dr. Heather Dean, University of Manitoba: personal communication, 1996).

Time Trend for CJD in Canada

To examine the incidence of reports over time, the mortality data were age-standardized. Figure 4 shows the mortality rate for CJD in Canada, standardized to the 1979 population.

There is a trend of increasing mortality over time, as the age-adjusted mortality rate increases from 1.1 deaths per million population in 1979 to 2.1 per million in 1992. The increase is most marked from 1986 onward. This may be related to increased case recognition at the time that the CJD and human growth hormone relationship was noted. There may also be an actual increase in disease incidence, although this graph must be interpreted with caution because the absolute numbers are very small. The unadjusted annual rates for the period 1979 to 1993 remain between 0.6 and 1.1 cases per million population, consistent with estimates of incidence worldwide.

Conclusion

The epidemiology of CJD in Canada is not well defined because CJD data sources are limited to aggregated mortality data and the annual total case numbers are small. However, several projects have been initiated to provide further information on the transmission of CJD in Canada.

In 1985, a national registry was created to track any cases of CJD in human growth hormone recipients in Canada. This registry remains active, and physicians who note unexplained neurologic changes in persons

Figure 1
Creutzfeldt-Jakob disease in Canada, 1979—1993: Annual mortality by sex (n = 334)

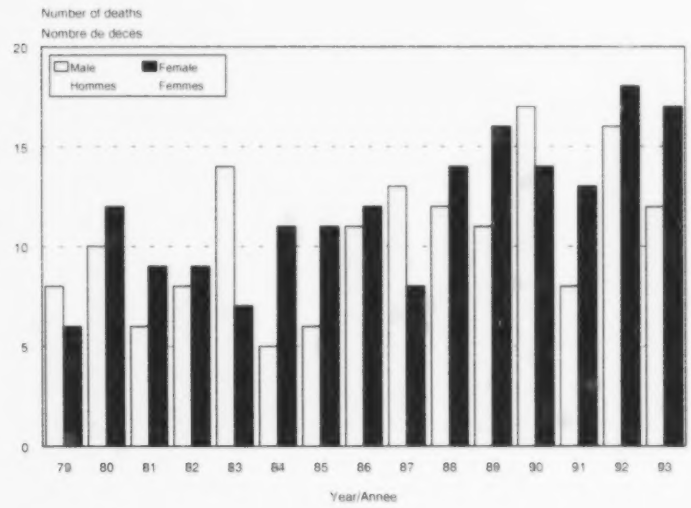
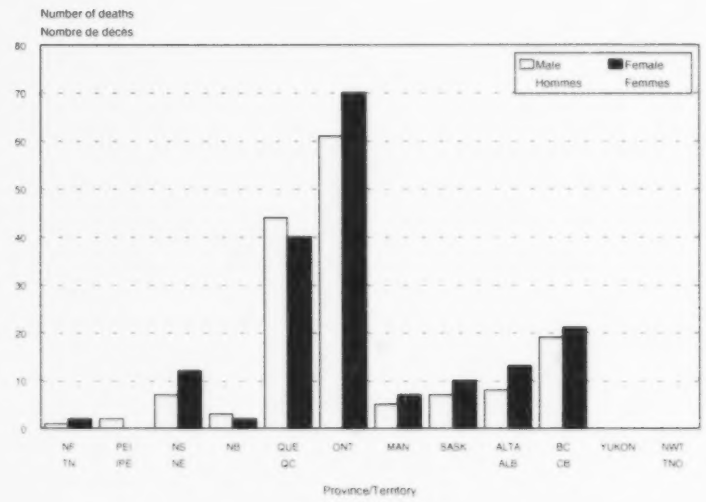


Figure 2
Creutzfeldt-Jakob disease in Canada, 1979–1993: Cumulative mortality by sex and province of residence at death



previously treated with human growth hormone are asked to notify Dr. Heather Dean, chair of the Canadian Growth Hormone Advisory Committee, University of Manitoba, tel.: (204) 787-4553 or (204) 787-7435.

In an effort to determine the risk of CJD through blood transfusions or organ transplants, the Laboratory Centre for Disease Control (LCDC) has proposed a number of investigative studies. These include a review of individual death certificates, active surveillance for CJD, a case-control study of CJD and blood, and a study for CJD in hemophiliacs (in collaboration with the Canadian Hemophilia Society). Neurologists will be asked to notify LCDC of any CJD patients seen in the last 5 years, including current patients, as a part of the active surveillance system.

Queries regarding CJD in blood may be directed to the Blood-borne Pathogens Division, Bureau of Infectious Diseases, LCDC, Health Protection Branch, Health Canada (tel.: (613) 954-5205; fax: (613) 952-6668).

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Figure 3
Age and sex distribution for Creutzfeldt-Jakob disease deaths in Canada, 1979–1993

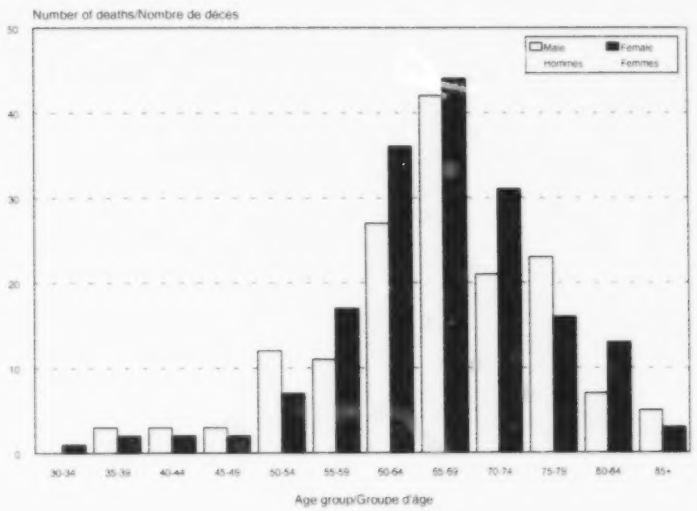
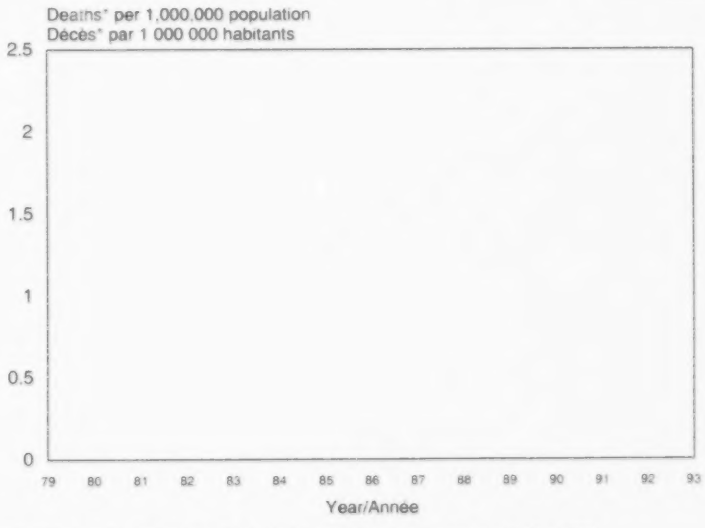


Figure 4
Age-adjusted mortality rate for Creutzfeldt-Jakob disease, Canada, 1979—1993



* Age-specific mortality rate for 1979 to 1992 x population in each age stratum for 1979

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Source: *E Stratton, BSc, BN, Field Epidemiologist, MN Ricketts, MD, MHSc, FRCPC, Medical Specialist, PR Gully, MB,ChB,FRCPC, Chief, Blood-borne Pathogens Division, Bureau of Infectious Diseases, LCDC, Ottawa.*

Editorial Comment

Recent events in the United Kingdom have raised the possibility that dietary factors may contribute to the risk of developing CJD. In March 1996, the government in the United Kingdom announced that a new pattern of CJD had been identified in a group of 10 patients with the disease; all were < 45 years of age at the time of onset of symptoms. The average age was 27. These patients had histologic features that differed from the sporadic, familial and iatrogenic forms of disease. No direct link has ever been made between CJD and the consumption of beef from cattle infected with bovine spongiform encephalopathy; however, UK investigators have now concluded that this new pattern of disease may suggest that such a link does exist.

A GASTROENTERITIS OUTBREAK AMONG CANADIAN TOURISTS IN MEXICO

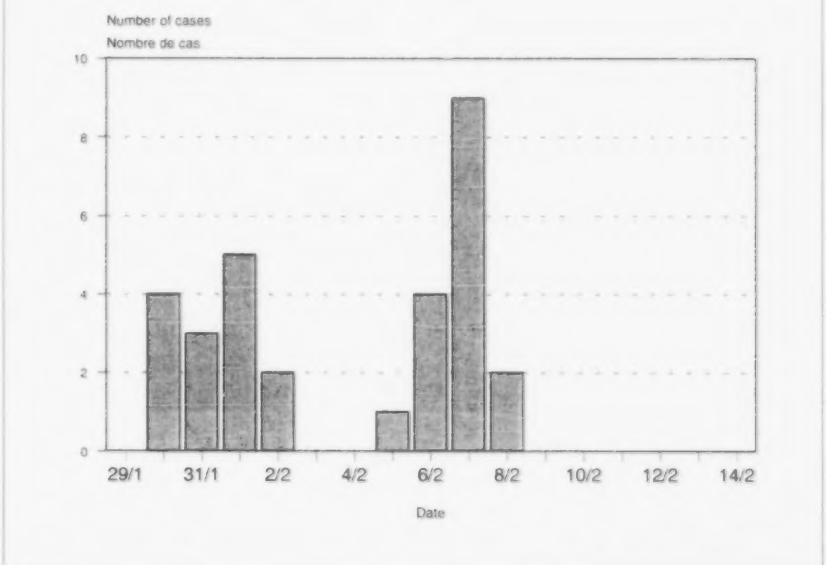
On 13 February, 1996, the Laboratory Centre for Disease Control, Health Canada, was notified about several cases of diarrhea among Canadians vacationing in Mexico. There was considerable concern because one of the tourists was quite ill and had to be airlifted back to Canada. On 15 and 16 February, 60 persons were randomly selected from a list of 124 passengers who had returned from Merida on 13 February to be interviewed by telephone to determine the extent and type of illness.

Thirty-four of the 60 persons were contacted; only one attempt was made to reach them. Thirty persons, from 23 households, had stayed at Resort A and all had been ill. The other four had stayed elsewhere in the area and none had become ill. Those who were ill ranged in age from 13 to 77 years (mean age: 48 years) and the majority (90%) were from Ontario.

Fifteen of the 30 cases had arrived at Resort A on 29 January (group 1) and the other 15 on 5 February (group 2). Following arrival at Resort A, the median onset time of illness for group 1 and 2 was 3 and 2 days, respectively (range: same day to 9 days later) (Figure 1). Twenty-nine cases had watery diarrhea; blood was present in the diarrhea of the remaining case. As of 15 February, the diarrhea has lasted from 1 to 17 days, with a median of 5 days. It was accompanied by gastrointestinal symptoms in most cases. In addition, almost two-thirds of the cases also experienced systemic symptoms. Nineteen of the cases had seen a physician in Mexico, six were given an antibiotic and one case required intravenous rehydration. No one was hospitalized. There have been no secondary cases reported in Canada.

The few questions concerning food indicated that more than 90% of the cases had drank only bottled water. Nobody had consumed water from any other sources, except when half of those interviewed were questioned about tea and coffee, they all indicated that they had consumed both beverages. All of the cases had eaten most of their meals at Resort A, mainly because there

Figure 1
Frequency of illness, by date of onset, in Canadian tourists staying at Resort A, 29 January – 13 February, 1996



was no other place to eat in this area. Ten cases had also eaten meals elsewhere during day trips.

As of 29 February, the only known laboratory-confirmed diagnosis was amoebiasis in two cases among the 34 persons interviewed. Many travellers returning from Resort A in early February visited a travellers' clinic in Montreal. *Campylobacter* spp. was isolated from the stool of at least four travellers from Montreal. A health unit in Ontario reported the isolation of *Campylobacter jejuni* from the stool of one woman who had stayed at Resort A from 29 January to 5 February. The mother of this woman, who was also at Resort A during the same period, had *Salmonella mbandanka* isolated from her stools. Moreover, *C. jejuni* was isolated from the stools of two other travellers from the area served by the Haldimand-Norfolk Regional Health Department who were at Resort A during the same period.

An environmental investigation was conducted in Mexico by public health authorities. Raw and cooked food as well as water samples were taken on 8 February. The samples showed that there was heavy coliform contamination in two-thirds of the 33 food items and dishes tested. *Salmonella* sp., *Yersinia enterolitica* and *Staphylococcus aureus* were isolated; unfortunately either no count or serotyping is available, making interpretation of these data difficult and limited. Tap and bottled water (one sample each) were free of contamination.

The most probable explanation for this outbreak is a continuous common source of infection. Multiple food vehicles and agents are suggested by the environmental and clinical microbiology results. Although water was not implicated by the environmental testing, only a few samples were taken.

All travellers to Mexico as well as any travellers to tropical countries should adhere strictly to all food and water precautions[1]. The most common sources of travellers' diarrhea are local water and fruits and vegetables prepared using this water. However, in this case, it is more likely that the prepared foods were contaminated.

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Source: *L Pelletier, MD, MPH, S Neamatullah, MD, R Mathias, MD, FRCPC, J Hockin, MD, MSc, Field Epidemiology Training Program, LCDC, Ottawa, Ontario; Direccion General de Epidemiologia, Mexican Health Authority, Merida, Mexico; Y Robert, MD, Centre de médecine de voyage du Québec, Montreal, Quebec; G Steen, CPHI, Haldimand-Norfolk Regional Health Department, Simcoe; J Cowell, CPHI, Brant County Health Unit, Brantford, Ontario.*

Editorial Comment

The preceding article describes an investigation of an outbreak of travellers' diarrhea that affected a large number of Canadian tourists visiting a resort in a Latin American location.

Diarrhea is one of the commonest illnesses associated with travel. It is estimated that some 30% of travellers to the tropical and semi-tropical regions of the world experience it[1,2]. Travellers' diarrhea has been described as a syndrome characterized by a two-fold or greater increase in the frequency of unformed bowel movements, often associated with abdominal symptoms[3,4], or as the occurrence of three or more watery or unformed stools per day during (or after) a journey, or any number of such stools accompanied by fever, abdominal cramps or vomiting[5].

High-risk tourist destinations include the developing countries and locations where water treatment and sewage systems are unreliable. In some high-risk locations in Africa, Asia and Latin America attack rates may approach 50%.

The etiology of travellers' diarrhea is diverse and is related both to the geographic area visited and the behaviour of the traveller. Enterotoxigenic *Escherichia coli* (ETEC) is a common causative organism accounting for 70% or more of the cases in Central America and Africa and 30% of those in Asia. Less common bacterial pathogens are *Salmonella*, *Campylobacter* and *Shigella*. Other organisms, such as *Aeromonas hydrophila*, vibrios, *Giardia lamblia* and *Entamoeba histolytica*, are associated with relatively few cases. No pathogenic organisms are isolated in one third to one half of the cases of travellers' diarrhea investigated.

Clinically, symptoms of travellers' diarrhea usually begin early in the journey[6]; in the largest proportion of those who become ill diarrhea begins around the third day. Normally the illness is self-limiting, with a duration of < 72 hours. Those who are < 40 years of age seem to recover more quickly. In 10% of those affected, however, symptoms persist for longer than 1 week.

Several prevention strategies exist for reducing the risk of acquiring the illness. These interventions are stratified by travel medicine practitioners according to the specific risks of the traveller[7]. Generally, these stratgies include education regarding dietary precautions (i.e., boil it, peel it, disinfect it or don't put it in your mouth) and consumption of bottled or purified water.

Routine antibiotic prophylaxis is not indicated for healthy travellers. Physicians may consider the use of prophylactic agents, either bismuth subsalicylate (Pepto-Bismol) or antibiotics, or immunization, depending upon the destination, duration of travel and behaviour of the traveller[8]. Physicians caring for the immunosuppressed patient should consider the additional risks associated with such situations[9].

The foregoing report indicates that travel-associated diarrheal disease remains a significant risk for travellers even in areas routinely visited by Canadians. Even relatively short-lived illness can have a significant impact on a 7- or 10-day vacation. This example reinforces the importance of adequate pre-travel medical advice and counselling regarding the risks of the disorder and the provision of information on preventive measures[10]. Travellers should be advised to exercise caution in the selection and preparation of water, food and dairy products.

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Announcement

LABORATORY BIOSAFETY PRINCIPLES AND PRACTICES
18-20 June, 1996

presented by the Office of Biosafety
Laboratory Centre for Disease Control, Health Canada

This is a course in laboratory safety, its principles and practices, as they relate to safety in the biomedical laboratory. It will offer the students current information and the opportunity to discuss problems in laboratory safety with experts in the field.

The course is accredited by the Canadian College of Microbiologists and the Canadian Society of Laboratory Technologists for continuing education credits.

It will be held at the Chateau Laurier, 1 Rideau Street, Ottawa, Ontario. A block of rooms has been reserved, until 1 June, at the government rate at Les Suites, 130 Besserer Street.

The closing date for registration is **15 May**. **Register early** because the number of registrants will be limited to 50 and the course may be closed to further registration prior to this date. The fee is **$400.00 (Cdn)**.

Additional information and application forms may be obtained from the **Office of Biosafety, Laboratory Centre for Disease Control, Tunney's Pasture (0700A1), Ottawa, Ontario K1A 0L2 [Tel.: (613) 957-1779; FAX: (613) 941-0596]**.

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